<Bioinformatics Training Unit> Genome Informatics

Bioinformatics Center
- Bioinformatics Training Unit -

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Scope of Research

Evolutionary studies based on molecular biology is called “molecular evolutionary biology”, which is one of the origins of the current bioinformatics. Living organisms have acquired wide variety of functions during the course of the evolution by changing the information encoded by the genomes. Inversely, reconstruction of the evolutionary history related to the functions would bring us a great insight into the acquired functions and the life. Furthermore, such evolutionary information is useful for practical fields such as drug design and proteins engineering. We develop new methodologies with evolutionary information, to extract biological knowledge from various molecular biological data including sequence and structure data of individual genes and proteins, genome data, and expression profile data. We also analyze the data of molecular biology from the evolutionary viewpoint, to obtain novel biological knowledge.

Research Activities (Year 2005)

Presentations

Computational Analysis of Substrate Specificity of Disaccharide-Specific Glycosidase., Daiyasu H, Mizutani M, Saitoh H, Sakata K, Toh H (Medical Institute of Bioregulation, Kyushu University), 5th Annual Metting of Protein Science Society of Japan, 30 June.

Evolutionary Analysis of Proteins Relevant to Quorum sensing., Ichihara H, Kuma K, Toh H (Medical Institute of Bioregulation, Kyushu University), 5th Annual Metting of Protein Science Society of Japan, 1 July.

Improvement in the Accuracy of Multiple Sequence Alignment Program MAFFT., Katoh K, Kuma K, Miyata T (JT Biohistory Resarch Hall, Waseda University), and Toh H (Medical Institute of Bioregulation, Kyushu University), 5th Int’l Workshop on Bioinformatics and Systems Biology, 22 August, Berlin.

Construction of Phylogenetic Tree Database for the Gene Families Involved in the Signal Transduction., Kuma K, Hirose N (Graduate School of Science, Kyoto University), Toh H (Medical Institute of Bioregulation, Kyushu University), Iwabe N (Graduate School of Science, Kyoto University), The 28th Annual Meeting of the Molecular Biology Society of Japan, 7 December.

Dualen: An Extraordinary Non-LTR Retrotransposon Family Encoding Dual Endonucleases., Kojima K, Fujiwara H (University of Tokyo), 77th Annual Meeting of the Genetics Society of Japan, 28 September.

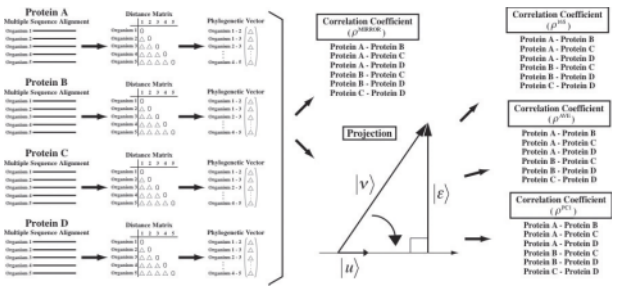
Comparison of Prediction Methods for Protein-Protein Interactions Using Co-evolutionary Information., Sato T, Yamanishi Y (Centre de Geostatistique , Ecole des Mines de Paris), Ichihara H, Kanehisa M, Toh H (Medical Institute of Bioregulation, Kyushu Univ.), 16th International Conference on Genome Informatics (GIW2005), 19 - 21 December.

Topics

The former Professor Hiroyuki Toh resigned on 31 March 2005.

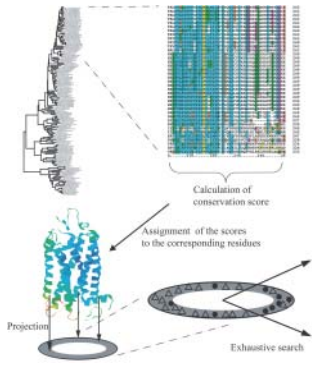
The Inference of Protein-Protein Interactions by Co-evolutionary Analysis is Improved by Excluding the Information about the Phylogenetic Relationships

The prediction of protein-protein interactions is currently an important issue in bioinformatics. The mirror tree method uses evolutionary information to predict protein-protein interactions. However, it has been recognized that predictions by the mirror tree method lead to many false positives. The incentive of our study was to solve this problem by improving the method of extracting the co-evolutionary information regarding the protein pairs. We developed a novel method to predict protein-protein interactions from co-evolutionary information in the framework of the mirror tree method. The originality is the use of the projection operator to exclude the information about the phylogenetic relationships among the source organisms from the distance matrix. Each distance matrix was transformed into a vector for the operation. The vector is referred to as a 'phylogenetic vector'. We have proposed three ways to extract the phylogenetic information: (1) using the 16S rRNA from the same source organisms as the proteins under consideration, (2) averaging the phylogenetic vectors and (3) analyzing the principal components of the phylogenetic vectors. We examined the performance of the proposed methods to predict interacting protein pairs from *Escherichia coli*, using experimentally verified data. Our method was successful, and it drastically reduced the number of false positives in the prediction.



Prediction of Interfaces for Oligomerizations of G-protein Coupled Receptors

Several lines of biochemical and pharmacological evidence have suggested that some G-protein coupled receptors (GPCRs) form homo oligomers, hetero oligomers or both. The GPCRs oligomerizations are considered to be related to signal transduction and some diseases. Therefore, an accurate prediction of the residues that interact upon oligomerization interface would further our understanding of signal transduction and the diseases in which GPCRs are involved. One of the complications for such a prediction is that the interfaces differ with the subtypes, even within the same GPCR family. Focusing on the distribution of residues conserved on the molecular surface in a particular subtype, we developed a new method to predict the interface for the GPCR oligomers, and applied it to several subtypes of known GPCRs to check the sensitivity. Subsequently, we found that predicted interfaces of rhodopsin, D_2 dopamine receptor and b_2 adrenergic receptor agreed with the experimentally suggested interfaces, despite difference in the interface region among the three subtypes. Moreover, a highly conserved residue detected from the D_2 dopamine receptor corresponded to a residue involved in a missense change found in the large family of myoclonus dystonia. Our observation suggests the possibility that the disease is caused by the disorder of the oligomerization, although the molecular mechanism of the disease has not been revealed yet. The benefits and the pitfalls of the new method will be discussed, based on the results of the applications.



Grants

Kuma K, A Study of Relationship between Mammalian Specific Features and Gene Diversification on the Basis of Genome Comparisons., Grant-in-Aid for Scientific Research (C), April 2005 - March 2007.

Kojima K, Acquiring New Function and the Evolution of Survival Strategy of Non-LTR Retrotransposons, Grant-in-Aid for Scientific Research for JSPS Researcher, 1 April 2005 - 31 March 2006.

Awards

Nemoto W and Toh H, Award in The 14th ScreenTech & TargetTalk 2005, Prediction of GPCR Oligomer Interface, IBC Life Sciences, 21 - 23 March, USA.

Nemoto W and Toh H, Poster Award in Int'l Biophysics Congress, Prediction of Interfaces for Oligomerization of GPCRs, IUPAB & EBSA & SFB & CNB, 28 August - 1 September, France.